Remarks

Claims 39-42, 48-51, 54-56, 67-73, 75, 78-80, 82-84, 86, 88-90, 92, 93 and 95, 96, 98-174 and 176-179 are presently pending in the subject application.

Reconsideration and allowance in view of the above amendments and the following remarks are respectfully requested.

Claims 97 and 175 have been canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a future continuing application.

Claims 40, 67, 69, 70, 75, 79, 80, 84, 89, 90, 96, 98, 101, 143, 147, 151, 152, 157-169, 173, 174, 176 and 177 have been amended herein to substitute the language "of the same length and fully complementary to" for the language "perfectly complementary to".

Claims 67, 75, 84, 147, 158, 162, 166 and 173 have been amended herein to indicate that the primer oligonucleotides of these claims include an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within the corresponding target nucleotide base sequence region of *Mycobacterium* nucleic acid under amplification reaction conditions. These and other claims have also been amended to indicate that the target region may be an RNA equivalent of the recited sequence or sequences. Support for these amendments can be found in, for example, the "Definitions" section of the specification at page 6, line 15 *et seq.*, and in the "Examples" section of the specification.

Claim 96 has been amended to incorporate the limitations of claim 97.

Claims 143, 158, 166 have been amended to remove reference to SEQ ID NO: 7 and its complement.

Claim 145, which formerly depended from claim 143, has been converted into an independent claim and amended to incorporate the limitations of unamended claim 143.

Claim 159 has been amended to remove reference to SEQ ID NO: 8 and its RNA equivalent.

Claim 167 has been amended to recite that the entire nucleotide base sequence of the claimed probe hybridizes to the recited region.

Claim 177 has been amended to recite a hybridization probe, where the entire nucleotide base sequence of the probe hybridizes to a region of *Mycobacterium* nucleic acid consisting of the nucleotide base sequence of SEQ ID NO: 8, the RNA equivalent thereof, or a sequence of the same length and fully complementary thereto.

Various of the claims have also been amended in a non-limiting manner to correct typographical errors and to ensure consistent phraseology in the claims.

Claims 178 and 179 are newly added.

New claim 178 is an independent claim and recites an oligonucleotide which consists of or is contained within the nucleotide base sequence of SEQ ID NO: 7 and an optional sequence recognized by an RNA polymerase.

New claim 179 is an independent kit claim which recites a primer oligonucleotide, where the entire nucleotide base sequence of the primer hybridizes to a region of *Mycobacterium* nucleic acid consisting of the nucleotide base sequence of SEQ ID NO: 7, the RNA equivalent thereof, or a sequence of the same length and fully complementary thereto. New claim 179 is an amended form of claim 166 prior to amendment herein.

In accordance with the provisions set forth in 37 C.F.R. § 1.121, a marked-up version of the amendments to the specification and claims is enclosed herewith.

Priority Data

The Examiner has invited Applicants to amend the specification to include priority data, if priority under 35 U.S.C. § 120 based on previously filed, co-pending applications is desired. In response, Applicants have updated the priority data in this application consistent with their Response dated September 29, 1998 and the priority data set forth in their Combined Declaration and Power of Attorney filed on April 3, 2002.

Drawing Correction

In response to the Form PTO 948 mailed on July 10, 1996, Applicants note that a formal drawing was transmitted to the Drafting Review Branch on November 21, 2002.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 40, 50, 51, 54, 67-73, 75, 78-80, 82, 83, 96-99, 101 and 143-177 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner contends that Applicants use of the phrase "the sequence perfectly complementary thereto" is subject to several interpretations and, therefore, is unclear. Without addressing the merits of the Examiner's argument, Applicants have amended the relevant claims in the manner suggested by the Examiner to indicate that the sequences being compared are of the same length and are fully complementary to each other. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Fourth Paragraph

Claim 73 stands rejected by the Examiner under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form. In making this rejection , the Examiner contends that a primer oligonucleotide having a nucleotide base sequence consisting of or contained within the nucleotide base sequence of SEQ ID NO: 1 or SEQ ID NO:19 is not supported by claim 67, from which claim 73 depends indirectly. In response to this rejection, Applicants have amended claims 71 and 73 to delete reference to SEQ ID NO: 19. However, Applicants observe that a primer oligonucleotide having the nucleotide base sequence of SEQ ID NO: 1 shares 22 contiguous 3' nucleotide bases in common with the nucleotide base sequence of SEQ ID NO: 22 and includes a 5' promoter sequence. Thus, a primer oligonucleotide having the nucleotide base sequence of SEQ ID NO: 1 is from 10 to 100 nucleotide bases in length and will hybridize to the complement of SEQ ID NO: 22 under amplification reaction conditions, thus meeting all of the limitations of claim 67. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(e)

Claims 96, 143, 158, 159, 166, 167, 175 and 177 stand rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Shah *et al.* (U.S. Patent No. 5,521,300). In support of this rejection, it is the Examiner contention that SEQ ID NO: 7 of the present invention corresponds to bases 11-34 of SEQ ID NO: 84 of Shah, and that SEQ ID NO: 8 of the present invention corresponds to bases 19-41 of SEQ ID NO: 48 of Shah. Applicants believe that the Examiner intended to state that there is overlap between SEQ ID Nos. 7 and 8 of the present invention and SEQ ID Nos. 48 and 56 of Shah, respectively. Applicants submit that this rejection is overcome by the amendments to the claims herein, each of which is explained under the Remarks section above. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

Claims 67, 68, 71, 75, 78, 84, 88, 147-149, 153, 158, 162, 166 and 173 stand rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by either of Products O 0629 or O 8629 of the 1990 Sigma Chemical Company Catalog. Without addressing the merits of the Examiner's argument, Applicants submit that this rejection is overcome by amendments to the claims herein, specifying that an at least 10 contiguous nucleotide base sequence of each claimed primer oligonucleotide hybridizes to an at least 10 contiguous nucleotide base sequence contained within the target nucleotide base region of *Mycobacterium* nucleic acid under amplification reaction conditions. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

Claims 39, 40, 67-71, 84, 86, 88, 150, 158, 162 and 173 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Boddinghaus *et al., J. Clin. Microbiol.*, 28:1751 (1990), taken in view of Suzuki *et al., J. Bact.*, 170(6):2886 (1988). Applicants respectfully traverse this rejection for the reasons that follow.

Boddinghaus is cited by the Examiner for teaching the usefulness of specific probes and primers targeting ribosomal RNA (rRNA). Based on this teaching, the Examiner contends that Boddinghaus motivates and suggests the generic use of such probes and primers in hybridization assays or PCR methods for Mycobacterial detection, provided sequence differences sufficient to give specificity to such assays are available. The Examiner does not suggest that Boddinghaus discloses any relevant sequence differences or any of the presently claimed probe or primer sequences.

Suzuki is cited by the Examiner for disclosing the entire 16S rRNA sequence of *Mycobacterium bovis* BCG, and the corresponding sequences of *Escherichia coli* and *Streptomyces lividan.* The Examiner states that the nucleotide base sequences of SEQ ID Nos. 2 and 3 and the complement of SEQ ID NO: 22 are present in the *M. bovis* sequence disclosed in Figure 2 of Suzuki. These regions, the Examiner urges, have specificity characteristics when compared with the corresponding sequences of *E. coli* and *S. lividan.* From this, the Examiner concludes that a skilled artisan at the time of the instant invention would have been motivated to design probes and primers in these regions with a reasonable expectation that such probes and primers would "perform as specific primers and/or probes for selective Mycobacteria assays". However, the Examiner does not contend that Suzuki discloses a probe or primer according to the present invention.

In order to demonstrate motivation for designing probes and primers to the regions noted by the Examiner, Applicants submit that there must be some suggestion provided in a reference or combination of references for priming and probing the regions specifically identified by the Examiner. In Suzuki, the sequence comparisons were not intended to facilitate the identification of regions for priming or probing for an organism of interest, and the stated objective of Boddinghaus was to distinguish between various groups of mycobacteria. Moreover, the Examiner has not identified any suggestion in the references that probes and primers for distinguishing between *M. bovis* BCG, *E. coli* and *S. lividan* would be useful, and no clinically relevant reason for distinguishing between these organisms has been articulated by the Examiner. Therefore, Applicants respectfully

submit that the Examiner's patentability analysis improperly relies upon hindsight reconstruction in attempting to make out a *prima facie* case of obviousness. Accordingly, withdrawal of this rejection is respectfully requested.

Objected to Claims

Claims 89, 90, 92 and 93 stand objected to by the Examiner as being dependent upon a rejected base claim, but are indicated to be allowable if rewritten in independent form, including all the limitations of the base claim and any intervening claim. Because Applicants believe that all presently pending claims should be allowable for the reasons set forth above, Applicants respectfully decline the Examiner's invitation to amend the noted claims at this time.

Allowable Claims

Applicants note with appreciation the Examiner's indication that claims 41, 42, 48, 49, 55, 56, 95, 100 and 102-142 are allowed.

Conclusion

Applicants submit that the subject application is in condition for allowance and Notice to the effect is respectfully requested.

Please charge any fees due in connection with this Reply to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Mailing

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on the date indicated below with the U.S. Postal Service as first class mail addressed to the Commissioner for Patents, Washington, D.C. 20231.

Respectfully submitted,

Dated: January 28, 2003 By: _____

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Marked-Up Version of Amendments

IN THE SPECIFICATION:

The specification has been amended in the first sentence on page 1 as follows:

This application is a divisional of U.S. Application Serial No. 08/345,861, filed November 28, 1994, now U.S. Patent No. 5,766,849, which is a continuation of U.S. Application Serial No. 07/925,405, filed August 4, 1992, now abandoned, which is a continuation-in-part of U.S. Application Serial No. 07/855,732, filed March 19, 1992, now U.S. Patent No. 5,399,491, which is a continuation-in-part of U.S. Application Serial No. 07/550,837, filed July 10, 1990, now U.S. Patent No. 5,480,784, which is a continuation-in-part of U.S. Application Serial No. 07/379,501, filed July 11, 1989, now abandoned, all of which applications are hereby incorporated by reference herein in their entirety.

IN THE CLAIMS:

The claims have been amended as follows:

39. (Five Times Amended) A kit for use in amplifying [*Mycobacterial*] *Mycobacterium tuberculosis* nucleic acid, said kit containing:

a first oligonucleotide comprising the nucleotide base sequence of xGCCGTCACCCCACCAACAAGCT (SEQ ID NO: 22); and

a second oligonucleotide comprising the nucleotide base sequence of xGGGATAAGCCTGGGAAACTGGGTCTAATACC (SEQ ID NO: 2),

wherein x is nothing or is a sequence recognized by an RNA polymerase, and wherein each said oligonucleotide is from 22 to [about] 100 bases in length.

40. (Five Times Amended) An oligonucleotide for use in amplifying *Mycobacterium tuberculosis* nucleic acid, said oligonucleotide being [of] from 22 to [about] 100 nucleotide bases in length and comprising the nucleotide base sequence of xGCCGTCACCCCACCAACAAGCT (SEQ ID NO: 22) or [the] a sequence [perfectly] of the same length and fully complementary thereto, wherein x is nothing or is a sequence recognized by an RNA polymerase.

41. (Six Times Amended) A kit for use in amplifying and detecting [*Mycobacterial*] *Mycobacterium tuberculosis* nucleic acid, said kit containing:

a first oligonucleotide of from 24 to [about] 100 nucleotide bases in length and comprising the nucleotide base sequence of SEQ ID NO: 3; and

a second oligonucleotide of from 22 to [about] 100 nucleotide bases in length and comprising [a] the nucleotide base sequence [selected from the group consisting] of xGCCGTCACCCCACCAACAAGCT (SEQ ID NO: 22) [and] or xGGGATAAGCCTGGGAAACTGGGTCTAATACC (SEQ ID NO: 2), wherein x is nothing or is a sequence recognized by an RNA polymerase.

42. (Six Times Amended) A kit for use in amplifying and detecting [*Mycobacterial*] *Mycobacterium tuberculosis* nucleic acid, said kit containing:

a first oligonucleotide of from 23 to [about] 100 nucleotide bases in length and comprising the nucleotide base sequence of SEQ ID NO: 8; and

a second oligonucleotide of from 20 to [about] 100 nucleotide bases in length and comprising [a] the nucleotide base sequence [selected from the group consisting] of xCCAGGCCACTTCCGCTAACC (SEQ ID NO: 23) [and] or xCGCGGAACAGGCTAAACCGCACGC (SEQ ID NO: 7), wherein x is nothing or is a sequence recognized by an RNA polymerase.

49. (Four Times Amended) The kit of claim 48 further comprising a third oligonucleotide having a 3' end which is unmodified, wherein said third oligonucleotide is from 20 to [about] 100 nucleotide bases in length and comprises [a] the nucleotide base sequence [selected from the group consisting] of xCCAGGCCACTTCCGCTAACC (SEQ ID NO: 23) [and] or xCGCGGAACAGGCTAAACCGCACGC (SEQ ID NO: 7), wherein x is nothing or is a sequence recognized by an RNA polymerase, and wherein the nucleotide base sequences of said second and third oligonucleotides are different.

67. (Four Times Amended) A primer oligonucleotide [of from 10] up to 100 nucleotide bases in length which hybridizes to a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 22, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto, and wherein said primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said region.

68. (Three Times Amended) The primer oligonucleotide of claim 67, said primer oligonucleotide being from 15 to 50 nucleotide bases in length.

69. (Three Times Amended) The primer oligonucleotide of claim 67, said primer oligonucleotide comprising the nucleotide base sequence of SEQ ID NO: 22 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

70. (Four Times Amended) The primer oligonucleotide of claim 67, wherein the nucleotide base sequence of said primer oligonucleotide consists of or is contained within the nucleotide base sequence of SEQ ID NO: 22 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

72. (Four Times Amended) The primer oligonucleotide of claim 71, said primer oligonucleotide comprising [a] the nucleotide base sequence [selected from the group consisting] of SEQ ID NO: 1 [and SEQ ID NO: 19].

73. (Four Times Amended) The primer oligonucleotide of claim 71, wherein the nucleotide base sequence of said primer oligonucleotide consists of or is contained within [a] the nucleotide base sequence [selected from the group consisting] of SEQ ID NO: 1 [and SEQ ID NO: 19].

75. (Four Times Amended) A composition for [amplification of] use in amplifying *Mycobacterium tuberculosis* nucleic acid, said composition comprising:

a first primer oligonucleotide consisting of an oligonucleotide [of from 10] up to 100 nucleotide bases in length which hybridizes to a first nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said first region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO:23, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto, and wherein said first primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said first region; and

a second primer oligonucleotide consisting of an oligonucleotide [of from about 10 to about] up to 100 nucleotide bases in length which hybridizes to a second nucleotide base sequence

region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said second region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 7, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto, and wherein said second primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said second region.

79. (Five Times Amended) The composition of claim 75 further comprising a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length which hybridizes with specificity to at least 10 contiguous bases of a third nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid to form a detectable duplex under reaction conditions, wherein the nucleotide base sequence of said third region is [the] selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 8, the RNA equivalent thereof, and [or the sequence perfectly] sequences of the same length and fully complementary thereto.

80. (Three Times Amended) The composition of claim 79, wherein said probe comprises [a] the nucleotide base sequence [selected from the group consisting] of SEQ ID NO: 8 [and the] or a sequence [perfectly] of the same length and fully complementary thereto.

84. (Four Times Amended) A composition for [amplification of] use in amplifying *Mycobacterium tuberculosis* nucleic acid, said composition comprising first and second primer oligonucleotides, each of said primer oligonucleotides being [from about 10 to about] up to 100 nucleotide bases in length,

wherein said first primer oligonucleotide hybridizes to a first nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, and wherein the nucleotide base sequence of said first region is selected from the group consisting

of the nucleotide base [sequence] sequences of SEQ ID NO: 22, the RNA equivalent thereof, and [or the sequence perfectly complementary thereto] sequences of the same length and fully complementary thereto, and wherein said first primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said first region, and

wherein said second primer oligonucleotide hybridizes to a second nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, and wherein the nucleotide base sequence of said second region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 2, the RNA equivalent thereof, and [or the sequence perfectly complementary thereto] sequences of the same length and fully complementary thereto, and wherein said second primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said second region.

89. (Three Times Amended) The composition of claim 84 or 86 further comprising a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length which hybridizes with specificity to at least 10 contiguous bases of a third nucleotide base sequence region [of] present in *Mycobacterium tuberculosis* nucleic acid to form a detectable duplex under reaction conditions, wherein the nucleotide base sequence of said third region [consists of] is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 3, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto.

90. (Twice Amended) The composition of claim 89, wherein said probe comprises the nucleotide base sequence of SEQ ID NO: 3 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

96. (Three Times Amended) A probe mix comprising:

a hybridization probe of from 10 to 100 nucleotide bases in length which hybridizes with specificity to at least 10 contiguous bases of a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid to form a detectable hybridization duplex under reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 8, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto; and

a helper oligonucleotide consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO: 10.

98. (Twice Amended) A probe mix comprising:

a hybridization probe of from 10 to 100 nucleotide bases in length which hybridizes with specificity to at least 10 contiguous bases of a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid to form a detectable hybridization duplex under reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 3, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto; and

a helper oligonucleotide.

100. (Four Times Amended) A kit for use in amplifying [*Mycobacterial*] *Mycobacterium tuberculosis* nucleic acid, said kit containing:

a first oligonucleotide comprising the nucleotide base sequence of xCCAGGCCACTTCCGCTAACC (SEQ ID NO: 23); and

a second oligonucleotide comprising the nucleotide base sequence of xCGCGGAACAGGCTAAACCGCACGC (SEQ ID NO: 7),

wherein x is nothing or is a sequence recognized by an RNA polymerase.

101. (Four Times Amended) A composition [useful in the detection] for use in detecting the presence of *Mycobacterium tuberculosis* in a sample, said composition comprising:

a) a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of a first nucleotide base sequence region [of a target] present in *Mycobacterium tuberculosis* nucleic acid, wherein the nucleotide base sequence of said first region is selected from the group consisting of [a] the nucleotide base [sequence selected from the group consisting] sequences of SEQ ID NO: 3[,] and SEQ ID NO: 8, the RNA equivalents thereof, and [the sequence perfectly] sequences of the same length and fully complementary thereto; and

b) a primer oligonucleotide of from [about] 10 to [about] 100 nucleotide bases in length which hybridizes to a second nucleotide base sequence region [of] present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said second region is selected from the group consisting of [a] the nucleotide base [sequence selected from the group consisting] sequences of SEQ ID NO: 2, SEQ ID NO: 7, SEQ ID NO: 22[,] and SEQ ID NO: 23, the RNA equivalents thereof, and [the sequence perfectly] sequences of the same length and fully complementary thereto.

143. (Three Times Amended) An oligonucleotide for use in amplifying *Mycobacterium tuberculosis* nucleic acid, said oligonucleotide being [of] from 20 to [about] 100 nucleotide bases in length[, said oligonucleotide] and comprising [a] the nucleotide base sequence [selected from the group consisting] of xCCAGGCCACTTCCGCTAACC (SEQ ID NO: 23)[, xCGCGGAACAGGCTAAACCGCACGC (SEQ ID NO: 7), and sequences perfectly] or a sequence of the same length and fully complementary thereto, wherein x is nothing or a sequence recognized by an RNA polymerase.

145. (Three Times Amended) A composition comprising:

a first oligonucleotide [in accordance with said oligonucleotide of claim 143, wherein said first oligonucleotide has] having a 3' end which is not modified to reduce or block extension of said first oligonucleotide by a polymerase; and

a second oligonucleotide [in accordance with said oligonucleotide of claim 143, wherein said second oligonucleotide has] having a 3' end which is modified to reduce or block extension of said second oligonucleotide by a polymerase, wherein each of said first and second oligonucleotides comprises a nucleotide base sequence selected from the group consisting of the nucleotide base sequences of xCCAGGCCACTTCCGCTAACC (SEQ ID NO: 23), xCGCGGAACAGGCTAAACCGCACGC (SEQ ID NO: 7), and sequences of the same length and fully complementary thereto, wherein x is nothing or a sequence recognized by an RNA polymerase.

147. (Three Times Amended) A primer oligonucleotide [of from 10] up to 100 nucleotide bases in length which hybridizes to a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 23, the RNA equivalent thereof, and [or the sequence perfectly] sequences of the same length and fully complementary thereto, and wherein said primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said region.

149. (Twice Amended) The primer oligonucleotide of claim 147, wherein said primer oligonucleotide is from [about] 20 to [about] 100 nucleotide bases in length.

150. (Twice Amended) The primer oligonucleotide of claim 69, wherein said primer oligonucleotide is from 22 to [about] 100 nucleotide bases in length.

151. (Three Times Amended) The primer oligonucleotide of claim 147, wherein said primer oligonucleotide comprises the nucleotide base sequence of SEQ ID NO: 23 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

152. (Three Times Amended) The primer oligonucleotide of claim 147, wherein the nucleotide base sequence of said primer oligonucleotide consists of or is contained within the nucleotide base sequence of SEQ ID NO: 23 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

157. (Twice Amended) The composition of claim 101 further comprising a helper oligonucleotide comprising a nucleotide base sequence selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 9[,] and SEQ ID NO: 10, and [the] sequences [perfectly] of the same length and fully complementary thereto.

158. (Twice Amended) A kit comprising a primer oligonucleotide [of from about 10 to about] up to 100 nucleotide bases in length which hybridizes to a nucleotide base sequence region [of] present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of [a] the nucleotide base [sequence selected from the group consisting] sequences of [SEQ ID NO: 7,] SEQ ID NO: 22[,] and SEQ ID NO: 23, the RNA equivalents thereof, and [the] sequences [perfectly] of the same length and fully complementary thereto, and wherein said oligonucleotide primer includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said region.

159. (Twice Amended) A composition comprising a specifically detectable nucleic acid hybrid formed under reaction conditions between a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid, or a sequence [perfectly] of the same length and fully

complementary thereto, and a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of said region, or [the] a sequence [perfectly] of the same length and fully complementary thereto, wherein the nucleotide base sequence of said region is [a] selected from the group consisting of the nucleotide base [sequence selected from the group consisting] sequences of SEQ ID NO: 3, [SEQ ID NO: 8, and] the RNA [equivalents] equivalent thereof, and sequences of the same length and fully complementary thereto.

160. (Twice Amended) A composition [useful in the detection of] for use in detecting the presence of *Mycobacterium tuberculosis* in a sample, said composition comprising:

a) a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of a first nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under reaction conditions, wherein the nucleotide base sequence of said first region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 3, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto; and

b) a primer oligonucleotide of from [about] 10 to [about] 100 nucleotide bases in length which hybridizes to a second nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said second region is selected from the group consisting the nucleotide base sequences of SEQ ID NO: 22[,] and SEQ ID NO: 2, the RNA equivalents thereof, and sequences [perfectly] of the same length and fully complementary thereto.

161. (Twice Amended) The composition of claim 160 further comprising a helper oligonucleotide comprising a nucleotide base sequence selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 4[,] and SEQ ID NO: 5, and [the] sequences [perfectly] of the same length and fully complementary thereto.

162. (Twice Amended) A kit comprising a primer oligonucleotide [of from about 10 to about] up to 100 nucleotide bases in length which hybridizes to a first nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said first region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 22, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto, and wherein said primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said first region.

163. (Twice Amended) A composition comprising a specifically detectable nucleic acid hybrid formed under reaction conditions between a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid, or a sequence [perfectly] of the same length and fully complementary thereto, and a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of said region, or [the] a sequence [perfectly] of the same length and fully complementary thereto, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 3, [or] the RNA equivalent thereof, and sequences of the same length and fully complementary thereto.

164. (Twice Amended) A composition [useful in the detection] for use in detecting the presence of *Mycobacterium tuberculosis* in a sample, said composition comprising:

a) a hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of a first nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under reaction conditions, wherein the nucleotide base sequence of said first region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 8, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto; and

b) a primer oligonucleotide of from [about] 10 to [about] 100 nucleotide bases in length which hybridizes to a second nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said second region is [a nucleotide base sequence] selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 23[,] and SEQ ID NO: 7, the RNA equivalents thereof, and [the] sequences [perfectly] of the same length and fully complementary thereto.

165. (Twice Amended) The composition of claim 164 further comprising a helper oligonucleotide comprising a nucleotide base sequence selected from the group consisting the nucleotide base sequences of SEQ ID NO: 9[,] and SEQ ID NO: 10, and [the] sequences [perfectly] of the same length and fully complementary thereto.

166. (Twice Amended) A kit comprising a primer oligonucleotide [of from about 10 to about] up to 100 nucleotide bases in length which hybridizes to a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of [a] the nucleotide base [sequence] sequences [selected from the group consisting] of SEQ ID NO: 23,[SEQ ID NO: 7,] the RNA equivalent thereof, and [the] sequences [perfectly] of the same length and fully complementary thereto, and wherein said primer oligonucleotide includes an at least 10 contiguous

nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said region.

167. (Twice Amended) A composition comprising a specifically detectable nucleic acid hybrid formed under reaction conditions between a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid, or a sequence [perfectly] of the same length and fully complementary thereto, and a hybridization probe [of from about] at least 10 [to about 100] nucleotide bases in length, wherein [comprising a] the entire nucleotide base sequence of said probe [which] hybridizes with specificity to [at least 10 contiguous bases of] said region, or the sequence perfectly complementary thereto, and wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 8, [or] the RNA equivalent thereof, and sequences of the same length and fully complementary thereto.

168. (Twice Amended) The kit of claim 41 further comprising a helper oligonucleotide comprising a nucleotide base sequence selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 4[,] and SEQ ID NO: 5, and [the] sequences [perfectly] of the same length and fully complementary thereto.

169. (Twice Amended) The kit of claim 42 further comprising a helper oligonucleotide comprising a nucleotide base sequence selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 9[,] and SEQ ID NO: 10, and [the] sequences [perfectly] of the same length and fully complementary thereto.

173. (Amended) The kit of claim 162 further comprising a second primer oligonucleotide [of from about 10 to about] up to 100 nucleotide bases in length which hybridizes to a second nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under amplification reaction conditions, wherein the nucleotide base sequence of said second region

is [the nucleotide base sequence] selected from the group consisting of the nucleotide base sequences of SEQ ID NO: 2, the RNA equivalent thereof, and [or the sequence perfectly] sequences of the same length and fully complementary thereto, and wherein said second primer oligonucleotide includes an at least 10 contiguous nucleotide base sequence which is fully complementary to an at least 10 contiguous nucleotide base sequence contained within said second region.

174. (Amended) The kit of claim 166, wherein the nucleotide base sequence of said region is the nucleotide base sequence of SEQ ID NO: 23 or [the] a sequence [perfectly] of the same length and fully complementary thereto.

176. (Amended) A hybridization probe of from [about] 10 to [about] 100 nucleotide bases in length comprising a nucleotide base sequence which hybridizes with specificity to at least 10 contiguous bases of a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under reaction conditions, wherein the nucleotide base sequence of said region is selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 3, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto.

177. (Amended) A hybridization probe [of from about] at least 10 [to about 100] nucleotide bases in length, wherein the entire [comprising a] nucleotide base sequence [which] of said probe hybridizes with specificity to [at least 10 contiguous bases of] a nucleotide base sequence region present in *Mycobacterium tuberculosis* nucleic acid under reaction conditions, wherein the nucleotide base sequence of said region is [the] selected from the group consisting of the nucleotide base [sequence] sequences of SEQ ID NO: 8, the RNA equivalent thereof, [or the sequence perfectly] and sequences of the same length and fully complementary thereto.